Drugs available as adjuncts to diet and exercise for treatment of obesity

Generic name	Usual dosing (adults)	US DEA schedule	Adverse effects and precautions*
Pancreatic lipase inhibitor approved for long-term use			
Orlistat	120 mg three times daily with fat-containing meals. A reduced dose of 60 mg[¶] is an option for patients who do not tolerate 120 mg.	Not a controlled substance	Cramps, flatulence, fecal incontinence, oily spotting, absorption of fat-soluble vitamins may be reduced. Rarely reported: severe liver injury, oxalate-kidney injury. Contraindicated during pregnancy.
Serotinin-2C receptor agonist approved for long-term use			
Lorcaserin	10 mg twice daily; re-evaluate after 12 weeks.	C-IV	Headache, dizziness, nausea, dry mouth, constipation (non-diabetic patients). Hypoglycemia, headache, back pain, cough (diabetic patients). Avoid in patients with severe hepatic or renal insufficiency (CrCl <30 mL/min). Preferably avoid use with other serotoninergic agents (including most antidepressants, triptan anti-migraine medications, 5HT3-antagonist antiemetics, tramadol, dextromethorphan, and some muscle relaxants) due to risk of serotonin toxicity. Neuropsychiatric side effects and valvulopathy were not significantly increased in clinical trials, but few long-term safety data are available. Contraindicated with ergot derivatives (eg, ergotamine) and during pregnancy. May cause psychic dependence and/or euphoria at higher than recommended doses. Possible increase in cancer risk based on murine model data.
Combination of phentermine-topiramate approved for long-term use			
Phentermine-topiramate	Initial: 3.75 mg phentermine/23 mg topiramate once daily in the morning for 14 days. Then titrate based upon response: 7.5 mg phentermine/46 mg topiramate daily for 12 weeks, then 11.25 mg phentermine/69 mg topiramate daily for 14 days. Maximum dose: 15 mg phentermine/92 mg topiramate daily; re-evaluate after 12 weeks.	C-IV (due to phentermine component)	Dry mouth, taste disturbance, constipation, paraesthesias, depression, anxiety, elevated heart rate, cognitive disturbances, insomnia (higher dose). Abuse potential due to phentermine component. Topiramate is teratogenic (increased risk of oral cleft defects, T1); negative pregnancy test prior to and during treatment and two forms of contraception necessary for women of child-bearing potential. Actions of topiramate component include inhibition of carbonic anhydrase; rarely metabolic acidosis and kidney stones may result from renal bicarbonate loss. Maximum dose with moderate hepatic or renal impairment (CrCl <50 mL/min) 7.5 mg phentermine/46 mg topiramate once daily. Upon discontinuation, tapering of dose over at least one week using every other day dosing is recommended. Contraindicated during pregnancy, hyperthyroidism, glaucoma, patients taking MAO inhibitors.
Combination of bupropion-naltrexone approved for long-term use			
Bupropion-naltrexone	Week 1: One tablet (8 mg naltrexone/90 mg bupropion) once daily. Week 2: One tablet twice daily. Week 3: Two tablets in morning and one tablet in evening. Week 4: Two tablets twice daily. Maximum daily dose: Four tablets (32 mg naltrexone/360 mg bupropion); re-evaluate after 12 weeks.	Not a controlled substance	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth. Transient increase in blood pressure (1 to 2 mmHg on average) during initial 12 weeks of treatment; heart rate may also be increased. Contraindicated in patients with uncontrolled hypertension, seizure disorder, eating disorder, use of other bupropion-containing products, chronic opioid use, use within 14 days of MAO inhibitors, pregnancy, or breastfeeding.[Δ]
GLP-1 agonist approved for long-term use			
Liraglutide	Initial: 0.6 mg subcutaneously daily. Increase at weekly intervals (1.2, 1.8, 2.4 mg) until recommended dose of 3 mg daily; re-evaluate after 16 weeks.[◇]	Not a controlled substance	Nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with T2DM (more common if used in conjunction with diabetes medications known to cause hypoglycemia), injection site reactions, increased lipase, increased heart rate. Rarely reported: pancreatitis, gallbladder disease, renal impairment, suicidal thoughts. Advise patients to avoid dehydration in relation to GI side effects. Monitor blood glucose in diabetic patients and adjust co-administered sulfonylureas (eg, reduce dose by 50 percent) and other anti-diabetic medications as needed to prevent potentially severe hypoglycemia. Causes a modest delay of gastric emptying.

			Use is not recommended in severe renal impairment (CrCl <30 mL/min), severe hepatic impairment, or children/adolescents ≤18 years and adults ≥75 years; safety and efficacy data are lacking. Possible increase in thyroid cancer risk based on murine model data. Contraindicated in pregnancy and in patients with a personal or family history of medullary thyroid cancer or multiple endocrine neoplasia 2A or 2B.
Noradrenergic sympathomimetic drugs approved for short-term use			
Benzphetamine	Initial: 25 mg once daily; may titrate up to 25 to 50 mg one to three times daily. Maximum dose: 50 mg three times daily.	C-III	Applies to all sympathomimetic agents: Due to their side effects and potential for abuse, we suggest **not** prescribing sympathomimetics for weight loss. If prescribed, limit to short-term (≤12 weeks) use. Adverse effects include increase in heart rate, blood pressure, insomnia, dry mouth, constipation, nervousness. Abuse potential due to amphetamine-like effects. May counteract effect of blood pressure medications. Avoid in patients with heart disease, poorly controlled hypertension, pulmonary hypertension, or history of addiction or drug abuse. Contraindicated in patients with a history of CVD, hyperthyroidism, glaucoma, MAO inhibitor-therapy, agitated states, pregnancy, or breast feeding.
Diethylpropion	Immediate release: 25 mg three times daily before meals. Controlled release: 75 mg every morning.	C-IV	
Phentermine	Immediate release: 15 to 37.5 mg daily or divided twice-daily. Orally disintegrating tablet (ODT): 15 to 37.5 mg once daily in the morning.	C-IV	
Phendimetrazine	Immediate release: 17.5 to 35 mg two or three times daily, one hour before meals. Maximum dose: 70 mg three times daily. Sustained release: 105 mg daily in the morning.	C-III	

CrCl: creatinine clearance; CVD: cardiovascular disease (arrhythmias, congestive heart failure, coronary artery disease, stroke, uncontrolled hypertension); GI: gastrointestinal; GLP-1: glucagon-like peptide 1; MAO inhibitors: monamine oxidase inhibitors; T1: first trimester pregnancy; T2DM: type 2 diabetes mellitus; US DEA: United States Drug Enforcement Agency; FDA: US Food and Drug Administration.

* Applies to all drugs except orlistat: May increase risk of hypoglycemia in type 2 diabetics. For additional information on potential interactions of anti-obesity drugs with other medications, use Lexi-Interact program included with UpToDate.

¶ Orlistat 60 mg is available without a prescription in the United States and some other countries.

Δ FDA recommends warning young adults (age 18 to 24 years) of the risk of becoming suicidal during initial treatment of psychiatric disorders with any antidepressant.

◇ According to United States labeling, if weight loss is not ≥4 percent after 16 weeks or 3 mg/week is not tolerated, discontinue use. Labeling in the European Union recommends discontinuation of use if weight loss is not ≥5 percent after 12 weeks of 3 mg/week.

Courtesy of authors.

With additional data from:

1. *dailymed.nlm.nih.gov/dailymed/index.cfm (Accessed October 8, 2014).*
2. *Kim GW, Lin JE, Blomain ES, Waldman SA. Antiobesity pharmacotherapy: new drugs and emerging targets. Clin Pharmacol Ther 2014; 95:1.*

Graphic 86204 Version 12.0